

## REMARKS

Upon entry of this amendment, claims 1-4, 10, 12, 36-39 and 43-45 will be pending in this application. Amended claim 1, 36 and 45 are fully supported by the specification at, for example, page 6, lines 10-16, and page 13, lines 3-11.

### I. The Claims Are Definite

Claims 1-4, 10, 12, 36-39 and 43-45 are rejected under 35 U.S.C. 112, second paragraph, for allegedly not being definite with respect to the limitation "without treating hyperhidrosis of the human subject". This limitation has been deleted from the claims, rendering the rejection moot. Thus, the claims are definite.

### II. Claims Are Not Obvious

As an overview, the claimed method for reducing wrinkle on a human face by administering a botulinum toxin using a needleless injector is not obvious because

- \* the claimed invention recites a step of a **deep** needleless injection of a botulinum toxin pass the dermis layer and into a muscle; and

- \* Vadoud-Seyedi et al. teaches away from such a deep needleless injection of botulinum toxin.

(A) The Office Action rejected claims 1, 2, 10, 12, 36, 37 and 43-47 under 35 U.S.C. section 103(a) as allegedly being obvious over Borodic (U.S. Patent 5,183,462, hereinafter "the Borodic reference"), Vadoud-Seyedi et al. (Dermatology 2000, 201(2): 179, hereinafter "the

Vadoud reference”) and Slate *et al.* (U.S. 6,645,169, earliest priority date June 8, 2000, hereinafter “the Slate reference”).

Specifically, the Office Action alleges that it would be obvious to

combine the three references to treat wrinkles and brow furrows by administering botulinum toxin A to muscles ... as taught by Borodic using needleless injector as taught by Vadoud-Seyedi *et al.*, and the injector can have sufficient pressure to deliver the medicament to the muscle tissue...as taught by Slate *et al.*...

Office Action, page 4.

Contrary to the Office Action’s allegation, there would be no motivation to combine the three references to arrive at the present invention. For example, the Vadoud reference teaches that a **needleless injection of botulinum toxin to the dermal layer of the hand for treating hyperhidrosis is not recommended** because such injection may damage superficial nerves; whereas a needleless injection to the dermal layer of foot for treating hyperhidrosis may be possible because the superficial nerves in the foot are “**deeper than their palmar homologues**”. Thus, it is clear that the Vadoud reference teaches away from injecting a botulinum toxin to the depth of where the superficial nerves are.

The claimed invention recites a step of needleless injection of the botulinum toxin to a muscle. **To administer to the muscle, it is necessary to make a deep injection of the botulinum toxin pass the superficial nerves, as the muscle is located underneath the dermal layer** (see previously submitted Exhibit A, Response of August 28, 2004). Thus, it is clear that the Vadoud reference teaches away from a needleless injection of a botulinum toxin to a muscle.

As the Vadoud reference teaches away from a needleless injection of a botulinum toxin to a muscle, one of ordinary skill would not be motivated to combine the Vadoud reference with the Borodic and Slate references to arrive at the claimed invention.

The Office Action further states that since the Borodic reference discloses the use of a needle syringe to inject botulinum toxin to a muscle, it would be obvious to substitute a needle syringe for a needleless syringe disclosed by the Vadoud reference. Applicant respectfully

asserts that the mechanism and fluid dynamics of a needleless injector is different from the needle syringe in such way that a needle syringe cannot be substituted by a needleless injector in every instance. For example, the Vadoud reference acknowledges that it is appropriate to administer a botulinum toxin to the hand using a needle syringe, but it may not be appropriate to use a needleless injector for administering to the hand. Thus, one of ordinary skill would not be motivated to substitute the needle syringe used in the Borodic reference for a needleless injector for treating a wrinkle on a human face.

(B) The Office Action rejected claims 3, 4, 38 and 39 under 35 U.S.C. section 103(a) as allegedly being obvious over the Borodic reference, the Vadoud reference, the Slate reference and McCabe et al. (U.S. Patent 5,525,510, hereinafter "the McCabe reference").

Claims 3, 4, 38 and 39 depend from the independent claims discussed above. Accordingly, these dependent claims are patentable over the cited references for the same reasons as discussed above. The additionally cited McCabe reference does not cure the deficiency of the Borodic, Vadoud and Slate references, because the McCabe reference is silent with respect to an administration of a botulinum toxin to the muscle.

In view of the foregoing, Applicant submits that the pending claims are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Respectfully submitted,



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Date: May 1, 2006

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